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BULLETIN OF
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ON THE THEORY OF BLOOD-TISSUE EXCHANGES: II. APPLICATIONS

LIEUT. R. E. SMITH AND ENS. M. F. MORALES, H-V(S), USNR*
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The application of a previously developed theory of inert gas absorption is here outlined. Interpretation of uptake curves and the method of obtaining tissue constants from such curves is discussed, together with illustrations from actual experiment. A critique of previous analytic procedures is included.

Introduction. In a previous paper (Smith and Morales, 1944), we have presented a theoretical treatment of inert gas absorption by the n tissues of a limb. It was there shown that the total amount of gas taken up to time t, $\phi(t)$, is given by:

$$\phi = C\left\{\left(V_0 + \frac{V_1}{\alpha_1} + \cdots + \frac{V_n}{\alpha_n}\right) - (Q_0\, e^{-k_0 t} + Q_1\, e^{-k_1 t} + \cdots + Q_n\, e^{-k_n t})\right\} = C\{\theta - \psi\} \tag{1}$$

where the A's, Q's, and k's are constants dependent upon certain physiological parameters: V_0, the blood volume; R, the delivery rate of blood flow; C, the delivery concentration of gas in the blood; and the volume V_i, blood surface, S_i, gas solubility, α_i, and permeability, h_i, of each tissue. It is our present concern to show how equation (1) and other implicates of the theory can be used in conjunction with experimental data.

Fitting and Interpreting Total Uptake Curves. Let us first consider the situation in which V_0, R, h_i, S_i, α_i, and V_i are constant. The problem of fitting is then the problem of obtaining the Q_j and the k_j from the smoothed experimental data.

* The material in this article should be construed only as the personal opinion of the writers and not as representing the opinion of the Navy Department officially.

Regrettably enough, it cannot be said that the procedure* as we use it, is effortless; however, it is perfectly straightforward and always yields results. We shall illustrate it for the important case in which n turns out to be 2:

1. First an asymptote is guessed, and so it is essential that the particular experiment be carried out long enough to permit this.

2. From this asymptote the experimental values of log ψ can be computed and plotted accurately on a large graph. In our experience this plot has the general nature suggested by the heavy line of Figure 1. It will be found that the "straightness" of the right-hand portion of the curve is exceedingly sensitive (0.25%) to the value chosen for the asymptote, and with a good initial guess, at most one trial is required to strike the proper figure.

3. The terminal portion of the line is taken to be the graph of $Q'e^{-k't}$, hence from this line extended and the experimental curve, it

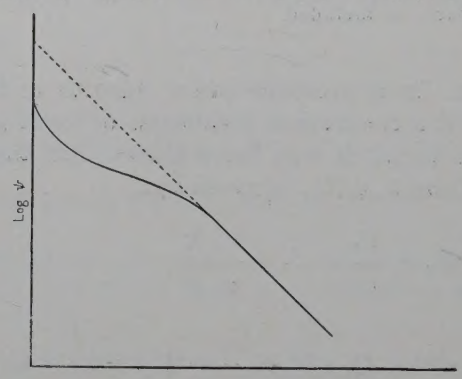

FIGURE 1

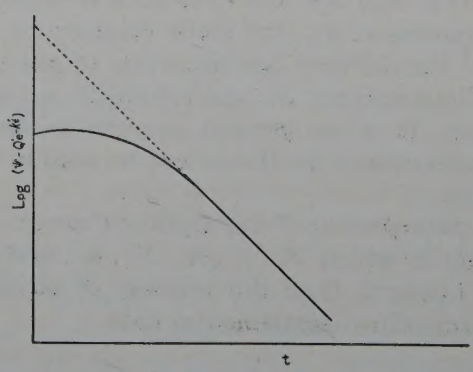

FIGURE 2

* Except in the fortunate but infrequent case of $n = 0$.

is possible to find $\psi - Q'e^{-k't}$. A plot is now made of the logarithm of this function. It has the general nature of Figure 2.

4. The terminal portion of this second plot is taken to be the graph of $Q''\ e^{-k''t}$ (where $Q'' < 0$). Hence from this line extended and the curve, log $(\psi - Q'e^{-k't})$, it is possible to get log $(\psi - Q'e^{-k't} - Q''e^{-k''t})$. When $n = 2$, this latter function turns out to be a straight line, and in fact represents $Q'''\ e^{-k'''t}$ (where $Q''' > 0$).

5. The foregoing procedure, if carried out with reasonable care, has yielded us results which fit the smoothed experimental curve throughout within the rather remarkable accuracy of better than 99%. Experimental data obtained by the authors and graphed in Figure 3

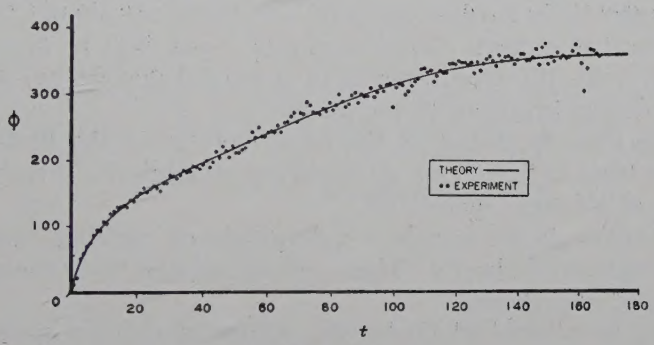

FIGURE 3

serves to illustrate this point. While we have not seen fit to do so, the precision of choice of fitting constants can then be increased by the standard method of alternation. Thus each component in turn is alternately computed when all the others are regarded as known. Such a process can be shown to converge on the best values of the constants. In any event the excellence of the fit, for any assumed n, is one justification of the theory.

A second method by which the theory can be tested has to do with the changing shape of $\phi(t)$ when the quantities, V_0, R, h_i, S_i, α_i, and V_i are changed, as few at a time as possible. How rapidly ϕ will reach its asymptote is governed chiefly by the k_j; therefore, a given physiological situation will cause the steady state to be reached rapidly or slowly according as it increases or decreases the k_j. The matter is schematized in Figure 4. It has been shown previously that increases in R, h_i, S_i, or α_i all tend to increase the k_j, while increases in V_0 or V_i tend to diminish them. We consider cases in which one or the other of these conditions will prevail:

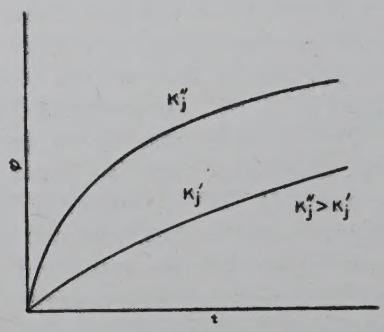

FIGURE 4

R is essentially cardiac delivery, and therefore should be proportional to cardiac output. Experimentally it can best be altered *alone* (to comply with the requirements of a partial derivative) by stimulating the vagus branches to the heart.

V_0, as already stated, is the blood volume of the limb in question. The local injection of epinephrine changes V_0 virtually independently of all other quantities.

V_s changes as we compare individuals of varying "build", say different degrees of obesity. These quantities and their measurement are discussed elsewhere.

h_s can be altered alone by the action of certain agencies, e.g. saponin or Ca^{++}.

S_s can not be altered alone save possibly in development (as distinct from growth).

α_s is altered for the case of fat as the *type* of fat deposited by the animal is changed.

The changes enumerated above constitute possible *tests* for the theory. Granting the theory, the logic can be reversed, and a change in $\phi(t)$ due to unknown causes can be analyzed. Such changes for instance are observed in fatigue or following arterial occlusion. It is obvious that in most of these instances more than one of the experimental parameters will be changing, consequently, in each case the graph must be judged specially. We are presenting such cases elsewhere.

Absolute Constants Obtained from Experimental Curves. Attention must be called to the important relation resulting from a previously established (Smith and Morales, *ibid*) Theorem II, viz., if the k_j are ordered, then any two successive k_j's set the upper and lower bounds of the quantity,

$$\alpha h \frac{S}{V}$$

for some one of the tissues. There is no particular difficulty in determining the experimental value of α for any tissue, once the nature of the continuous intracellular phase is known. Therefore, knowing either h or S/V it becomes possible to estimate the other. The quantity h of inert gases has been measured for high polymer membranes (Muller, 1941). The ingenious method of I. Gersh, as yet unpublished, yields values of S/V for various tissues. It is therefore possible to check and use the aforementioned relationships very readily. Such calculations will appear elsewhere. The *ratio* of the permeabilities of two different gases can be estimated precisely from experiments on the same individual using two different gases. In this application, suppose that α'_i, h'_i, S'_i/V'_i for the gas (′) has been found to lie between two known k's, and therefore have an approximate value, M'. If similar measurements for some other gas (″) are made, then:

$$\alpha'_i h'_i \frac{S_i}{V_i} \cong M',$$

$$\alpha''_i h''_i \frac{S_i}{V_i} \cong M'',$$

or,

$$\frac{h'_i}{h''_i} = \frac{\alpha''_i M'}{\alpha'_i M''}.$$

The foregoing techniques are other instances of situations where it is possible to glean information regarding cellular constants from experiments performed on the intact animal or human subject.

Other Equations. We shall close this paper with a note on other equations which have been used in the study of this same phenomenon.

The equation of H. W. Haggard (1924),

$$\int \frac{d\phi}{\phi(B-\phi)} = At, \quad A, B, \text{constants} \tag{2}$$

is frankly empirical, and as such has served a useful purpose, especially in studying the uptake of ethyl ether by men.

The equation of A. R. Behnke,

$$\int_0^t \frac{d\phi}{\phi^0 - \phi} = kt \quad \text{or} \quad \phi = \phi^0(1 - e^{-kt}) \tag{3}$$

was originally proposed* by Behnke as a provisional empirical equation, and in that capacity has been very successfully applied to the exchange of nitrogen in human subjects and in dogs. An attempt has been made, however, to give theoretical interpretation to this relationship, and such studies have been accepted widely enough to merit critical examination.

It is to be noted that equation (3) is a special case of equation (1), for $n = 0$, i.e., *for the case of a single absorbing phase.* That the body cannot, with respect to any gas, be considered as a single absorbing phase has of course been realized by all authors. However, it has been assumed that although the limb is a multiphase system, the various phases differ in their absorptive powers and therefore take up the gas in sequence, so that at any one stage equation (3) will hold, with ϕ^0 as the asymptotic amount of gas in the tissue.

First, there is a serious theoretical fallacy involved in this procedure, namely that a reaction cannot depress its rival unless the attending $\Delta \mu$ is vastly more negative than that of the rival, and such is not the case in this instance. This difficulty leads to a number of paradoxical consequences:

The "elimination constant" varies continuously over the range of time; so that there is little advantage to studying $k(t)$ instead of $\phi(t)$.

The average elimination constant for any one tissue is calculated over a period of time when presumably only that tissue is absorbing. Yet when these same elimination constants are used together, the stages during which these tissues are absorbing are found to overlap.

Q's sometimes turn out to be negative numbers, and therefore could not possibly represent amounts of gas.

Second, there is the important anatomical argument that the blood distribution of a limb is such that *some* blood is *at all times* the exclusive monopoly of any one type of tissue, hence it is unavoidable for tissues to absorb simultaneously. When (as has been done) the whole body uptake is considered, the situation is even more critical. For example, in the mesentery and in the retro-peritoneal region there are depots of fat which have their own vascular beds, completely independent of the blood supply to other phases.

Finally, it should be noted that an equation cannot reasonably be regarded as a theoretical interpretation until the constants which it involves are related to well-defined physical quantities. It is this limitation on the part of equation (3) that precludes the correlation of changes in experimental set-up with changes in "k".

* Personal communication.

Incorporated throughout this work is the generous counsel of Professors N. Rashevsky and A. S. Householder of the University of Chicago, and of Cmdr. A. R. Behnke, (MC), USN, and Lieut. I. Gersh, H-V(S), USNR, of this Institute, to all of whom the authors are gratefully indebted.

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ON THE THEORY OF BLOOD-TISSUE EXCHANGES: III. CIRCULATION AND INERT-GAS EXCHANGES AT THE LUNG WITH SPECIAL REFERENCE TO SATURATION

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The results of a simple analysis of the situation in the lungs with regard to the uptake of inert gases is presented. It is shown that the gas transfer at the lung governs the early stages of gas uptake by a body region so that the latter conceivably could be used as an index of lung function. It is shown that the so-called Fick Principle, which serves as the basis of most indirect cardiac output methods, is an approximation to a more general equation. When the latter equation is applied to a slowly permeating gas, it offers the possibility of determining functional lung surface.

Being the spatial intermediates between the atmosphere and all body tissues, the lung membranes potentially govern all inert gas exchanges.[1] It is, therefore, unavoidable that their role be included in such exchange theories as have been attempted (Smith and Morales, 1944a, hereinafter referred to as SM). Furthermore, the kinetics of inert gas exchange across the lung membranes has been made the basis for certain indirect studies of circulatory function, and so, from this point of view, a study of these kinetics has immediate practical application. In appreciation of these two incentives, the following note attempts to formulate certain transfer problems at the lung, and then to incorporate the solutions into more comprehensive theories and applications.

As must forever be the case in biology, the physical situation in the organism must be considerably simplified and schematized before the problem involving it can be formulated. For our present discussion the theoretical model is pictured in Figure 1. We imagine the entire pulmonary circulation to pass through a lung blood chamber of volume, V cm^3. The walls of this chamber are the lung membranes

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[1] This is not to imply that only lung membranes may pass an inert gas. Behnke (1941) has shown that N_2 can be exchanged by the skin in significant amounts. The same author (1938) has also demonstrated that He is passed by the bladder wall in very slight amounts.

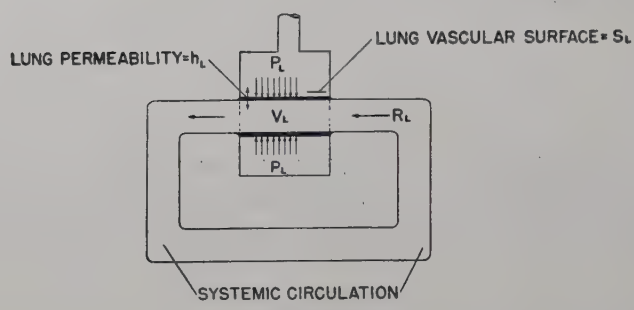

FIGURE 1

themselves. On the external side of the membranes the gas in question is assumed to exist at a *mean* constant pressure of p dynes cm^{-2}. The remaining symbolism is either obvious from Figure 1 or is consistent with that previously introduced (SM).

Gas exchanges at the lung can be divided conveniently into those processes which result in a net gain of gas by the body as a whole (saturation), and those processes and phases which result in a net loss (desaturation). Not only has the chief experimental concern of the authors been with the former process, but also the analysis of lung desaturation, even at the level presented here, is beset with a great many complications which at this point we have found it impossible to simplify. For these reasons the attention of this paper is focused on saturation phenomena, and mention of the converse process will be slight. Some measure of simplicity is attained by dividing saturation itself into certain temporal stages, and this accordingly has been done. We now turn to the processes themselves.

Saturation. The time course of saturation may be pictured as follows: At the instant that the subject takes the first breath of the gas, he builds up the alveolar pressure of the gas to the value p. We designate that instant as zero time. The blood at that moment in the lungs will then begin to flow out with a progressively increasing concentration of gas. Finally, the last part of that blood will flow out with a concentration of gas to be sustained for as long as $p =$ constant. This initial stage, equal to the length of time which blood spends in the lung, we may designate as stage (a). There will now follow a stage in which the arterial blood is carrying and delivering blood to the various absorbing regions, and during which the venous return does not yet carry gas. This stage (b) ends when the veins first[2] begin to return charged blood to the lung, and it is, therefore,

[2] Actually we will neglect the coronary return (about 5% of the total) which is the first such return.

equal in length to the least round trip time minus the lung time. From this time on there is a stage (c) during which more and more regions are contributing to the venous return, ending finally when the region with the longest round trip circulation time just begins to contribute to the venous return. From this instant on, for as long as the experiment is in progress, all regions are contributing to the venous return. We call this last stage (d). During each stage we will want to know: (1) the concentration x of the gas in the blood leaving the lung, (2) the concentration y of the gas in the blood arriving at the lung, (3) the uptake Φ and the rate of uptake Φ' of gas by the body as a whole during this stage. The time relations of the latter variables (3) are schematically depicted in Figure 2. The nature of the curves will be discussed in the analysis.

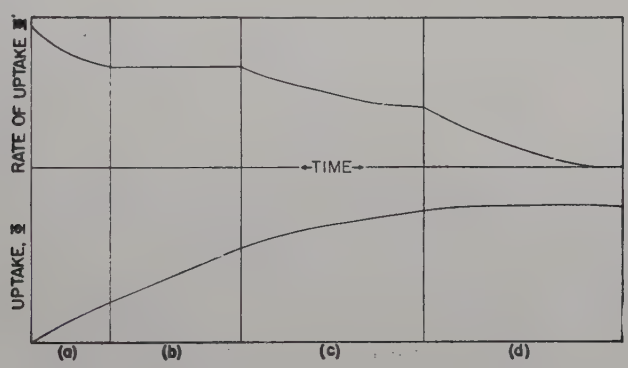

FIGURE 2

Stage (a). Letting x denote the concentration of the gas in the pulmonary veins at time t, we see that x will grow in time according to the same law as it would have grown had the blood in V been stagnant, the only difference between the two cases being that in the former instance x will never attain its asymptotic value, but will be cut short and kept at a reduced constant level. This follows easily from the equation for solution of the gas into the moving blood. Due to the fact that in the lung the blood flows rapidly through exceedingly fine vessels, we may assume that diffusion within the blood in a plane transverse to the axis of the vessel takes place instantaneously, while no diffusion takes place along the axis of the vessel at all. To this approximation, with k as the Henry's Law solubility constant,[3]

[3] This equation is actually derived by imagining the blood stream split into cylindrical elements of volume that flow through V at a rate such that R cms^3 will pass through V per second. The concentration of gas attained in each of these is then calculated, and from this, the concentration of gas in the emerging blood. Inherent in the latter step is the assumption that the ratio of surface to volume

$$V\,dx/dt = hS(kp - x). \tag{1}$$

Under the initial conditions, $x = 0$ when $t = 0$, we integrate equation (1) to give

$$x = kp(1 - e^{-hSt/V}), \text{ for } 0 \leqq t \leqq V/R. \tag{2}$$

Thus x starts from zero and rises to

$$x = kp(1 - e^{-hS/R}), \text{ for } V/R \leqq t, \tag{3}$$

at which value it will stay so long as p and R remain constant. During stage (a) the rate of uptake of gas is

$$\Phi'_{(a)} = Rx = Rkp(1 - e^{-hSt/V}), \tag{4}$$

and the uptake itself is

$$\begin{aligned}\Phi_{(a)} &= \int_0^t \Phi'_{(a)}dt = \int_0^t Rkp(1 - e^{-hSt/V})\,dt \\ &= Rkp\left\{t - V(1 - e^{-hSt/V})/hS\right\}.\end{aligned} \tag{5}$$

Stage (b). Passing into the next stage we see that x remains at the value indicated by equation (3), whence

$$\Phi'_{(b)} = Rx = Rkp(1 - e^{-hS/R}), \tag{6}$$

and

$$\Phi_{(b)} = \left\{Rkp(1 - e^{-hS/R})\right\}\left(t - \frac{V}{R}\right). \tag{7}$$

Much importance attaches to stage (b) for two reasons. First, it represents the stage at which tissues commence to absorb gas, and second, it is the stage during which cardiac outputs are usually measured. We will digress to follow these two considerations.

It will be seen that the delivery concentration, $C^{(r)}$, at a distant region, r, will vary in the following way:

$$\begin{aligned}&C^{(r)} = 0, \text{ for } 0 \leqq t \leqq t_a^{(r)}, \\ &C^{(r)} = kp(1 - e^{-hSt/V}), \text{ for } t_a^{(r)} \leqq t \leqq t_a^{(r)} + V/R, \\ &C^{(r)} = kp(1 - e^{-hS/R}) = x(\infty), \text{ for } t_a^{(r)} + V/R \leqq t \leqq \infty,\end{aligned} \tag{8}$$

where $t_a^{(r)}$ is the "arterial time", or time taken for the blood to flow from the lung to the r-th absorbing region. Since in the normal mam-

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of an element, $\Delta S/\Delta V$, is the same as S/V. To the extent that all blood vessels are roughly cylindrical save at junctions, this assumption would seem justified. We are also tacitly assuming that the flow of blood is frictionless since we assert that a local concentration can be sustained despite the streaming of the blood.

mal both $t_a^{(r)}$ and V/R are a matter of seconds (see Kvale and Allen, 1939, and Schmidt, 1941), as contrasted with a gas saturation time of over three hours (Smith and Morales, 1944b), it is not unreasonable to suppose that $C^{(r)}$ builds up instantaneously to $x(\infty)$, although this is of course not strictly the case. However, in certain situations, of which a most important one is pulmonary edema, or again in shock, both $t_a^{(r)}$ and V/R may be significantly lengthened due to an impaired circulation. In such cases $C^{(r)}$ can no longer be considered constant in the early stages of absorption. These facts have a certain bearing on the gas exchange of a limb, and more specifically, on the shape of the limb absorption curve. Thus, the differential equations governing absorption in the r-th region are (SM)

$$V_0^{(r)}\, dx_0^{(r)}/dt = R^{(r)}\, C^{(r)} - R^{(r)}\, x_0^{(r)} - \sum_{i=1}^{i=n} h_i S_i (x_0^{(r)} - x_i^{(r)}),$$

$$\cdots\cdots\cdots\cdots\cdots\cdots \qquad (9)$$

$$V_i^{(r)}\, dx_i^{(r)}/dt = h_i S_i^{(r)} (x_0^{(r)} - x_i^{(r)}),$$

and the total uptake up to time t is

$$\phi^{(r)} = V_0^{(r)}\, x_0^{(r)} + V_1^{(r)} x_1^{(r)} + \cdots + V_n^{(r)}\, x_n^{(r)}, \qquad (10)$$

while

$$\phi' = R^{(r)} (C^{(r)} - x_0^{(r)}).$$

The early variation in $C^{(r)}$ can be taken into account exactly by solving equation (9) in stages as prescribed by equation (8). While that is not a formidable problem, its explicit solution is fairly tedious, and for the time being we have not the experimental equipment rapid enough to verify the result on normal animals. However, the general quantitative description of this phenomenon is easily perceived with the aid of equation (10). For when $t = 0$, $x_0^{(r)} = 0$, so that $\phi'^{(r)}(0)$ is equal to $R^{(r)}\, C^{(r)}$. In the *approximation,* $C^{(r)} =$ constant > 0, so that $\phi'^{(r)}(0) > 0$; in the *exact solution,* $C^{(r)}(0) = 0$, so that $\phi'^{(r)}(0) = 0$. Since in either case $\phi'^{(r)}(\infty) = 0$, while $\phi'^{(r)}(t) > 0$, $(0 < t < \infty)$, it follows from Rolle's theorem that the exact solution for $\phi'^{(r)}(t)$ passes through at least one maximum, and, therefore, that $\phi^{(r)}(t)$ passes through at least one inflection. These relationships are depicted schematically in Figure 3. In a number of uptake curves we* have found it to be the case that a hint of an inflection occurred within the first minute of absorption. *It is to be inferred from the above that*

* Since this paper was written we have had the opportunity to discuss this matter with Dr. C. Tobias of the University of California. He too had observed this phenomenon in several carefully determined curves and had successfully demonstrated their reproducibility some years ago, but his work has unfortunately remained unpublished. The presence of this inflection as a very early test of lung dysfunction remains a very interesting possibility.

such an inflection will be accentuated and will appear later whenever either or both pulmonary and systematic circulations are abnormally slow.

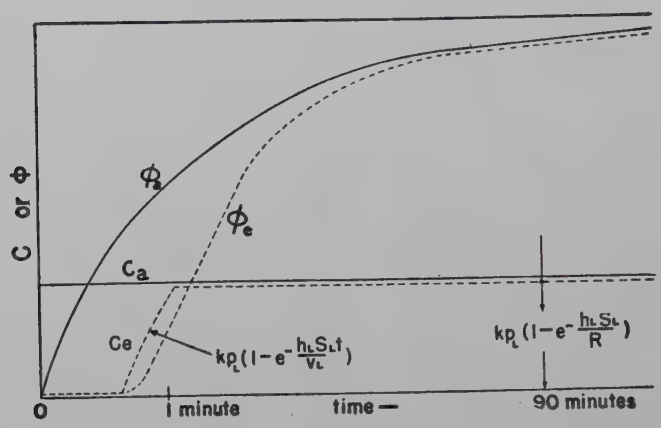

FIGURE 3

As remarked above, the most useful methods of determining cardiac output, namely those methods using an inert "foreign" gas such as acetylene, are put in operation in stage (b). In essence, these methods all depend upon the determination of Φ' from measurement on the rate at which the inert gas disappears from the spirometer, and simultaneous calculation of Φ' as $= Rx$.

A convenient method of doing this for continuously determinate gases has been communicated to us by Dr. H. B. Jones of the University of California:

Since, from a finite breathing mixture of oxygen and inert gas the respiration will progressively remove more oxygen than inert gas, the concentration of inert gas relative to the concentration of oxygen would normally increase in time. However, it is possible to determine experimentally how much oxygen per unit time must be added to the respirometer in order that the ratio of the concentrations of the two gases will remain constant.

If K^0 = initial volume of inert gas in the spirometer,
$v^0_{O_2}$ = initial volume of oxygen in the spirometer,
q = oxygen consumption per unit time,
β = oxygen addition per unit time,

then it can be easily shown that

$$\Phi = \frac{K^0 q}{v^0_{O_2}} t - \int_0^t \beta \, dt.$$

It has been found experimentally that during the stage (b), β is a constant; consequently, for this stage, we may write

$$\Phi = \left(\frac{K^0 q}{v^0_{O_2}} - \beta \right) t = \Phi' t,$$

where the coefficient of t is fully determined experimentally. Combining with equation (13):

$$R = \left(\frac{K^0 q}{v^0_{O_2}} - \beta \right) / kp .$$

In the same subject the quantities p and k can presumably be kept constant, and in that event, it follows that $(K^0 q / v^0_{O_2}) - \beta$ is a measure of cardiac output. Jones has used this measure clinically with encouraging results.

Then, of course,

$$R = \Phi' / x . \tag{11}$$

Substituting from equation (6), we see that *as long as we are truly in stage* (*b*),

$$R = \Phi' / kp (1 - e^{-hS/R}) = \text{cardiac output} . \tag{12}$$

Knowing the various constants and determining Φ' experimentally, we may solve equation (12) which is seen to be transcendental in R. However, if we *furthermore assume that* $e^{-hS/R}$ is negligible, then equation (12) reduces to

$$R = \Phi' / kp . \tag{13}$$

Actual methods make both assumptions (12) and (13), and so it becomes necessary to study these proposals and their verification.

It is be noted at the outset that at least for C_2H_2 Grollman (1932) has very conclusively proved[4] the truth of assumption (13) by comparing R values so calculated with R values obtained by the so-called direct heart puncture method. And it is a further suggestive fact that the errors introduced by the failure of the two assumptions tend to cancel each other (both numerator and denominator of (13) are smaller than they should be).

We may answer the question of neglecting the exponential by recourse to data in the literature. The basal level of R (Grollman, *ibid.*) is about 66 cms^3 sec^{-1}. The quantity S has been variously estimated to be 5 to 9×10^5 cms^2, of which measurements perhaps Willson's (1922) is the best, namely, 7×10^5 cms^2. Thus, even if h were of the order of 1×10^{-4} cm sec^{-1}, the error introduced by omitting the exponential would be under 5%. Actually, it is to be expected that h will be greater, because histological examination of the alveolar wall has failed to show the presence of a continuous plasma membrane

[4] However, there seems to be one condition which imperils even the conclusion of Grollman's direct heart-puncture method. Sjöstrand (1935) has gathered considerable evidence to show that the lung may contain variable blood depots whose contents are not at one time a part of the pulmonary flow. It is evident that if some of the gas inspired (as measured by the respirometer loss) over the trial period were absorbed by the depots, then the *A-V* oxygen difference divided into the respirometer loss would give values of R which are too high. This error would be inherent in *all* gas methods.

between the gas of the lumen and the blood (Maximow and Bloom, 1940). Translating the Kroghs' "diffusion constants" into absolute permeabilities, we have obtained[5]

$$h_{O_2} = 7.00 \times 10^{-3} \text{ cm sec}^{-1}; \; h_{CO_2} = 3.0 \times 10^{-4} \text{ cm sec}^{-1},$$

while for oxygen and carbon dioxide respectively, the $e^{-hS/R}$ values are .0000 and .0408. Thus, these two gases would be satisfactory in cardiac output measurement if they could be regarded as inert gases. In any event, it is clear that a determination of the h of the gas is prerequisite to deciding in favor of either equation (12) or (13). The latter equation, (13), has also another experimental implication. If one chooses a gas for which h is small, so that the exponential is not negligible, we obtain instead of expression (13) the following:

$$hS = R \log \frac{Rkp - \Phi'}{Rkp}.$$

The quantity Φ' for the gas is readily obtainable, while R can be determined either directly or by the acetylene method. From the above formula we may, therefore, compute hS, or if h can be independently obtained (as it can, although in a more difficult measurement), S, the *functional* (as distinct from morphological) surface area of the lung can be determined. This is a quantity not otherwise easily obtained, and has considerable importance in metabolic theory.

An interesting special case of gas absorption is suggested by M. Krogh (1914). For gases which are rapidly and irreversibly combined with some fixed constituent of the blood (e.g., hemoglobin), we have in stage (a)

$$x = x^0 + \frac{hSkp}{V} t, \tag{i}$$

where x^0 is the original concentration of gas in the blood. In stage (b) we reach

$$x(\infty) = x^0 + \frac{hSkp}{R}. \tag{ii}$$

The rate of uptake during stage (b) is then

$$\Phi' = hSkp, \tag{iii}$$

while the amount lost from the respirometer is

$$\Phi = (hSkp)t. \tag{iv}$$

On the other hand, the total amount present in the body is

$$(\text{Original amount}) + \Phi = vx^0 + (hSkp)t, \tag{v}$$

[5] See M. Krogh, 1914 and A. Krogh, 1919. It is interesting to note that the measure of permeability used by these authors is stated in terms of a pressure gradient across the membrane, while absolute permeabilities are written in terms of concentration (in solution) gradients. Due to its high water solubility, the h value of CO_2 is lower than that for oxygen, contrary to the widely held view. In our opinion, the latter is a more natural measure, since the gases certainly permeate only in solution.

where v is the total body blood volume. Relation (ii) can be made to be an equation for cardiac output, and the slope and intercept respectively of (v) can yield v and hS.

For pointing out a possible fallacy in this equation we are indebted to Lieutenant N. Pace, H-V(S), USNR. If the equilibrium between CO and HbCO so overwhelmingly favors the latter that *all* the CO available is consumed without exhausting the carrying power of the blood, then R could not be inferred from measurements on the disappearance of gas from the external circuit. This condition, however, seems unlikely in view of the fact that there is considerably more CO in the expired air than can be accounted for by "dead space".

Stage (c). With the onset of this stage, y, the concentration of gas in the pulmonary artery is no longer zero. The concentration in the pulmonary vein, $x(\infty)$, of course remains constant. Thus, we have

$$\Phi'_c = R[x(\infty) - y], \tag{14}$$

and

$$\Phi_c = Rx(\infty)(t - t_c^{(1)}) - R \int_{t_c^{(1)}}^{t} y dt. \tag{15}$$

Therefore, the chief problem lies in the determination of y. Let us proceed by arranging the N absorbing regions, $r = 1, 2, \cdots N$, in order of increasing (round-trip) circulation times. $t_c^{(r)}$, i.e.,

$$t_c^{(1)} < t_c^{(2)} \ldots < t_c^{(r)} \ldots < t_c^{(N)}.$$

Referring to zero time, it is clear that stage (c) commences at $t = t_c^{(1)}$, and ends at $t = t_c^{(N)}$. Blood arriving at any instant, t, from the r-th region brings a contribution from that region as of $t_v^{(r)}$ seconds back, at which time that region has been absorbing for $t - t_c^{(r)}$ seconds. Here we use $t_v^{(r)}$ to represent the "venous time", or blood flow time from the r-th region to the lung. If the blood in the vein draining the r-th region flows out at a rate of $R^{(r)}$ cm^3 sec^{-1}, and is charged to a concentration of $x_0^{(r)}$ gm cm^{-3}, then its contribution to the pulmonary artery concentration (when such blood arrives there) will be $(R^{(r)}/R)x_0^{(r)}$ gm cm^{-3}, and the amount which has arrived there from the r-th region will up to time t be

$$\int_{t_c^{(r)}}^{t} R^{(r)} x_0^{(r)} dt.$$

Substituting from equation (15), SM and integrating, this becomes

$$\begin{aligned} &R^{(r)}x(\infty) \int_{t_c^{(r)}}^{t} \left(1 - \sum_{j=0}^{j=n} A_{0j}^{(r)} e^{-k_j^{(r)}(t-t_c^{(r)})}\right) dt \\ &= R^{(r)}x(\infty) \left\{ (t - t_c^{(r)}) - \sum_{j=0}^{j=n} \frac{A_{0j}^{(r)}}{k_j^{(r)}} [1 - e^{-k_j^{(r)}(t-t_c^{(r)})}] \right\}. \end{aligned} \tag{16}$$

And combining expression (16) with (15), we see that for $t_c^{(m)} < t < t_c^{(m+1)}$,

$$\Phi_{(c)} = Rx(\infty)(t - t_c^{(1)}) - \sum_{r=1}^{r=m} R^{(r)}x(\infty)\left\{(t - t_c^{(r)}) - \sum_{j=0}^{j=n} \frac{A_{0j}^{(r)}}{k_j^{(r)}}[1 - e^{-k_j^{(r)}(t-t_c^{(r)})}]\right\}. \tag{17}$$

Thus, it is seen that in stage (c) the rate of uptake begins to decrease in a fashion which can be described by sums of exponentials. If the body could be regarded as consisting of only a few functional regions with radically different t_c's, then strictly speaking Φ_c would be a discontinuous curve during this stage; however, since there are many regions with not too different circulation times, the discontinuities are likely to be completely masked.[6] It may be noted that the greater the $k_j^{(r)}$ are, the more rapidly will Φ' vary during stage (c), and the greater will be the error introduced into a cardiac output measurement overlapping this time stage.

Stage (d) is easily disposed of by putting the upper limit of the summation in equation (17) as $r = N$. Theoretically as well as practically, $\Phi_{(a)}$ is a continuous curve. Combining the equations of stage (d) with previous work (SM) we see that the stage ends with

$$\begin{aligned} x_0^{(r)}(\infty) &= x(\infty), \\ x_i^{(r)}(\infty) &= x(\infty)/\alpha_i, \; i \neq 0, \\ \Phi'(\infty) &= 0, \\ \Phi(\infty) &= x(\infty)(\nu + \sum_{r=1}^{r=N}\sum_{i=1}^{i=n} V_i^{(r)}/\alpha_i). \end{aligned} \tag{18}$$

The state described by equation (18) is theoretically never reached, for Φ is asymptotic to $\Phi(\infty)$. However, within a few hours of gas uptake Φ is experimentally indistinguishable from $\Phi(\infty)$, and for practical purposes we speak of the body as being "saturated" with gas.

This completes our analysis of the saturation process.

Desaturation. If while equation (18) holds, p is suddenly reduced from $p =$ constant to $p = 0$, the entirety of the resulting processes is termed desaturation. In principle, this process is governed by the same general equations as its converse.

By solving equation (1) with $p = 0$, we have immediately the relationships between the concentration of gas in the pulmonary ar-

[6] Another agency which in actual practice ensures this occurrence is the mixing that results from the velocity profile within blood vessels. This has been referred to previously.

tery and the pulmonary vein:[7]

$$x = ye^{-(hS/V)t}, \qquad 0 < t < V/R,$$
$$x = ye^{-hS/R}, \qquad V/R < t. \tag{19}$$

The tissue discharge is still governed by equation (9) with appropriate boundary conditions. In particular, if $C^{(r)} = 0$, then

$$x_0^{(r)} = x(\infty)\,(A_{00}e^{-k_0t} + A_{01}e^{-k_1t} + \cdots + A_{0n}e^{-k_nt}). \tag{20}$$

As usual, the larger the k_j's the faster will be the variations in x_0.

Finally, dilution at the arterial end of the lung takes place according to the same law. Denoting by $x_0^{(r)}(t - t_v^{(r)})$ the value of $x_0^{(r)}$ $t_v^{(r)}$ seconds ago, then at time t the concentration of gas in the pulmonary artery is

$$\frac{1}{R}\sum_{r=1}^{r=m} R^{(r)}x_0^{(r)}(t - t_v^{(r)}). \tag{21}$$

What introduces a hopeless cumbersomeness into the analysis of desaturation is the fact that different regions have different circulation times; hence, all regions are always at different stages of discharge, and remain so for all time. In equation (19) the exponential appears alone, so that unlike the situation in equation (12), it cannot be disregarded (there is ample experimental evidence to support this assertion). More so than in the case of saturation, the existence of portal circulations precludes any such assumption as $t_c^{(i)} > t_c^{(j)}$ implying $t_a^{(i)} > t_a^{(j)}$. Thus, as a whole, any simplifications would be distinctly out of accord with experimental facts, and we have not seen fit to press the analysis further.

Notwithstanding the difficulties of interpretation, the desaturation phenomenon is clinically important, and has received considerable experimental attention. Interesting contributions have been made by Behnke (1935) on N_2, and by Underwood and Diaz (1941), who injected radon into the saphenous vein and by its radioactivity measured its appearance in the expired air. The latter authors present this data in the suggestive fashion of the plot, log $(-\Phi)$ vs. t. The experiments were carried out over four minutes, yielding an average point every minute. It is quite clear that in every graph shown, *the last three points lie on a good straight line, while the first is always displaced upward.* This would seem easily explainable in a qualitative way: On the first lung passage and before the next (roughly one minute), the loss is governed by expression (19) with only slight dilution.

[7] Note that equation (19), like equation (13), is an equation for functional surface area of the lungs.

On subsequent passages the main loss is still governed by (19), but with lowered concentration (due to complete mixing). Accessory losses to tissues are of course also present, and governed by expression (9). The value given for the first slope is about 0.69, not too different from, and lower than the hS/R computed above, as is to be expected. The subsequent stages involving tissue absorption are of course of a lower and uninterpretable slope.

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ON THE FORM AND STRENGTH OF TREES: PART II THE PRIMARY BRANCHES

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The main purpose of this note is to relate the shape of the branch to its strength and to explain by theory why a tree has a large number of branches.

1. The branch as a cantilever. If the weight of the secondary branches is taken into account by a suitable increase of the specific weight of the primary branch, a reasonable model of the primary branch is a horizontal cantilever of conical shape. (A model of a branch of maximum strength will be discussed in Part III.) If r' is the radius of the base of the cone, L the length of its axis, ρ' the ratio of the weight of the complete secondary branches to the primary branch, m' the ratio of the weight of the primary branch in green state to its weight when oven dry, the maximum bending stress, which occurs at the base of the cone, is (Timoshenko, 1940, pp. 88-93):

$$m'(1+\rho')GL^2/(3000r'). \tag{1}$$

where G is the specific gravity of oven dry wood. The units are throughout the paper kg and cm unless otherwise stated. Putting fraction (1) equal to σ_b/f', where f' is a safety factor and σ_b the maximum possible bending stress which is given by equation (3) of Part I, we get:

$$m'(1+\rho')f'L^2 = 3711000\, G^{1/4}\, r'. \tag{2}$$

Assuming that the safety factor is the same for all branches of the tree, we see that for a given species the length of the branch is proportional to the square root of the radius at the base. For the species grown in this country G varies between about 0.3 and 0.7 (U.S. Department of Agriculture, 1940, pp. 50-53), so that approximately $G^{1/4} = 0.75$ to 0.91. Taking for instance $m' = 2.5$, $\rho' = 0.6$, $f' = 84$, $G = 0.5$ so that $G^{1/4} = 0.84$, we get for $r' = 1$ cm, $L = 1$ meter.

In applying the theory to an actual branch it may be convenient, because of the irregular shape of the branch, to eliminate the length L

in relation (2) by means of the total weight of the branch. Therefore, calling B the weight of the primary branch in the state as it is obtained after being cut from the tree, that is, with all its secondary branches and leaves, we have

$$B = \pi m'(1 + \rho') G r'^2 L/3000 , \tag{3}$$

and from expression (2) we get:

$$f' B^2 = 4.07\, m'(1 + \rho') G^{9/4} r'^5 . \tag{4}$$

Or, if P is the weight of the primary branch alone in the green state, that is, without secondary branches and leaves, we have:

$$f'(1 + \rho') P^2 = 4.07\, m' G^{9/4} r'^5 . \tag{5}$$

2. The shape and the strength. We eliminate the radius r' in (4) by means of the lateral surface S of the primary branch. As Rashevsky (1943, p. 44) pointed out, S has a biological meaning, because in a first approximation one may assume S proportional to the area of the leaves and therefore proportional to the amount of substances exchanged by the branch with the surrounding air. Since for a cone of the size of a branch $1 + (r'/L)^2 = 1$ we have,

$$S = \pi r' L . \tag{6}$$

The elimination of r' in equation (4) by means of relations (3) and (6) gives:

$$10^{15}\, C B^3 = f'[m'(1 + \rho')]^4 G^{11/4} S^5 , \text{ where } C = 989 . \tag{7}$$

We attempt now to explain some shape characteristics of the tree by considerations of mechanical strength. To do this, we will have to compare with each other some shapes of branches and branch arrangements which are geometrically different but biologically identical. A reasonable mathematical condition for a biological identity is the constancy of G, m', ρ', B, and S, which will be assumed throughout the following discussion. It must be noted, however, that actually the weight B consists of two different parts: B_b = the weight of leaves and sapwood which have mainly a biological function, and B_m weight of the heartwood whose main function is to provide the tree with the necessary mechanical strength. The ratio B_b/B_m might be called the biological efficiency of the branch or of the tree. A mathematical condition for a biological identity would be B_b = const. rather than B = const. But if we include into the concept of biological identity the condition of equal biological efficiency, B_b = const. may be substituted by B = const.

We discuss now the following questions:

(I) *Why does the cross-section of a branch decrease towards the free end?* For a conical shape of a branch the safety factor f' is given by equation (7). For a branch in the shape of a circular cylinder we find, if we neglect the area at the free end in calculating S, the same equation (7) with $C = 195$. We see, therefore, that the conical shape makes the branch five times stronger.

(II) *Why does a tree have many branches?* Consider a tree with n conical branches and assume that the safety factor f' is the same for all branches. Call r'_i the radius of the base and L_i the length of the i-th branch. Instead of equations (2), (3), and (6), we have now the following equations:

$$r'_i = m'(1+\rho')f'L_i^2/(3711000\,G^{1/4}), \tag{8}$$

$$B = \pi m'(1+\rho')G\textstyle\sum_1^n r'^2_i L_i/3000, \tag{9}$$

$$S = \pi \textstyle\sum_1^n r'_i L_i, \tag{10}$$

where B is now the total weight and S the total lateral surface of all branches. If we eliminate r'_i in equations (9) and (10) by means of equation (8) and calculate B^3/S^5, we get equation (7) with $C = 989K$, where

$$K = (\textstyle\sum_1^n L_i^3)^5/(\sum_1^n L_i^5)^3 .$$

K is > 1 for $n > 1$, whatever are the values of the L_i's. This is an immediate consequence of Jensen's inequality (Hardy-Littlewood-Pólya, 1934, p. 28). Therefore, independently of the length of branches, a tree with n branches is K times stronger than a biologically equivalent one-branch-tree. To get an idea about the order of magnitude of K, we put $L_i = iL_1$. Then (Pascal, 1900, p. 235):

$$K = (27/16)(n^2+n)^4/(2n^2+2n-1)^3 .$$

Several values of K are given in the following table:

$n=1$	2	3	4	5	6	7	8	9	10	25
$K=1$	1.6	2.8	4.6	6.7	9.2	12.1	15.5	19.3	23.5	137

for $n \to \infty$, $K \to (27/128)n^2$.

In conclusion, one may say that the tree shows some kind of tendency to shape itself in such a manner as to increase its own strength. However, this may be a question of viewpoint only. In fact, if one compares a one-branch-tree with a n-branch-tree on the assumption that the strength is in both cases the same ($f' =$ const.), one finds [cf. equation (7)] that S is proportional to $K^{1/5}$, so that the large number of branches that a tree has may be interpreted also as a ten-

dency of the tree towards a higher biological efficiency. The increase of S is, however, much smaller than the increase of f' in the previous discussion, for instance, for $n = 25$ we have $K^{1/5} = 2.7$.

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THE TWO-FACTOR THEORY OF NERVOUS EXCITATION WITH NON-NORMAL ACCOMMODATION

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By introducing a parameter which vanishes when the accommodation is normal the modifications in theoretical predictions when accommodation is non-normal are discussed, particularly in the case of stimulation by alternating currents. It is found that non-normality always has the effect of lowering the optimal amplitude of the alternating current, measured in units of the observed rheobase.

Quantitative comparison of experimental results with predictions made by the Rashevsy-Hill two-factor theory of nervous excitation is always made with the assumption of normal accommodation, and no one seems to have considered in detail what is to be expected in case the accommodation is non-normal. It is true that the equations become quite complicated then, and the agreement is very good in a great many instances even with this restriction. On the other hand, there are deviations, especially with stimulation by alternating currents (Hill, 1936; Hill, Katz, and Solandt, 1936; Coppée, 1936) where the optimal amplitude of the stimulating current is rather less than predicted (Parrack, 1940), and it seems worth-while to inquire whether this deviation—and possibly others—can be attributed to non-normality of accommodation.

We shall suppose that the deviation from normality is never great, and we shall introduce a parameter for measuring this deviation and calculate the corrections of the first degree in this parameter in the case of stimulation by alternating currents. It is convenient to use Rashevsky's form of the equations and to introduce the *Hauptnutzzeit* as the unit of time. If we write y_1 and y_2 instead of ε and j, this, together with a suitable choice of units for measuring the y_i, enables us to write these equations in a normalized form (Householder, 1944);

$$y_i' + \mu_i(y_i - y_i^0) = e^{\mu_i} S, \tag{1}$$

with primes denoting the derivative and S representing the stimulus. If we write

$$\log(\mu_1/\mu_2) = \lambda = \mu_1 - \mu_2 + \nu, \tag{2}$$

then

$$\mu_1 = (\lambda - \nu)/(1 - e^{-\lambda}),$$
$$\mu_2 = (\lambda - \nu)/(e^{\lambda} - 1). \tag{3}$$

With $\nu = 0$ we should have normal accommodation. In general $\lambda > 0$.

The cathodal rheobase R_c (Hill's "observed rheobase", I_1), is found to be given by

$$\frac{y_2^0 - y_1^0}{R_c} = \left(\frac{1}{\mu_2} - \frac{1}{\mu_1}\right) - \left(\frac{e^{\mu_2}}{\mu_2} - \frac{e^{\mu_1}}{\mu_1}\right), \tag{4}$$

while that which Hill calls the "true rheobase", I_0, the rheobase in the absence of any accommodation, is given by

$$(y_2^0 - y_1^0)/I_0 = e^{\mu_1}/\mu_1 . \tag{5}$$

In the case of stimulation by alternating currents

$$S = I \sin \omega t , \tag{6}$$

and in the steady state

$$\begin{aligned} y_i - y_i^0 &= A_i I \sin(\omega t - \gamma_i), \\ A_i &= e^{\mu_i}(\omega^2 + \mu_i^2)^{-1/2}, \\ \sin \gamma_i &= \omega(\omega^2 + \gamma_i^2)^{-1/2}, \\ \cos \gamma_i &= \gamma_i(\omega^2 + \gamma_i^2)^{-1/2}. \end{aligned} \tag{7}$$

The difference

$$[(y_1 - y_1^0) - (y_2 - y_2^0)]/I$$

is expressible as a periodic function whose amplitude A is given by

$$A^2 = \frac{\omega^2(e^{\mu_1} - e^{\mu_2})^2 + (\mu_1 e^{\mu_2} - \mu_2 e^{\mu_1})^2}{(\omega^2 + \mu_1^2)(\omega^2 + \mu_2^2)}, \tag{8}$$

and for minimal stimulation,

$$AI = y_2^0 - y_1^0. \tag{9}$$

Since A is a function of ω, the least amplitude I necessary for stimulation is that value I_m obtained from equation (9) with A maximal. If we set

$$A = (e^{\mu_1} - e^{\mu_2})/B , \tag{10}$$

the maximal A is given by the minimal B.

We now set

$$F = (\mu_1 e^{\mu_2} - \mu_2 e^{\mu_1})/(e^{\mu_1} - e^{\mu_2}),$$
$$M_i^2 = \mu_i^2 - F^2, \quad \Omega^2 = \omega^2 + F^2, \tag{11}$$

which enables us to write

$$B^2 = (\Omega^2 + M_1^2)(\Omega^2 + M_2^2)\Omega^{-2} \tag{12}$$

and obtain easily the minimum

$$B = B_m \equiv M_1 + M_2\,, \quad \Omega_m^2 = M_1 M_2\,. \tag{13}$$

We note that F vanishes with ν, that M_i^2 differs from μ_i^2, and hence, M_i from μ_i only by terms of the second and higher orders in ν, and that Ω differs from ω to the same extent. With ν very small, this difference could become significant, but not otherwise, and we may regard the optimal frequency as independent of the normality of accommodation. Likewise, the symmetry of the graph of B (or of I) against the logarithm of ω (Hill, 1936) is unaffected except for small values of ν, and also the rectilinearity of the plot of B^2 (or I^2) against ω^2 for large ω. On the other hand, the plot of B^2 (or I^2) against ω^{-2} on the low-frequency side of the optimum should deviate from rectilinearity for sufficiently small values of ω.

We shall see, however, that non-normality of accommodation tends to diminish I_m where $\nu > 0$. We note first that Hill computes the ratio of I to the "true rheobase", I_0. Since, with sufficient approximation, $M_i = \mu_i$, we find from equations (5), (9), (10), and (2) that

$$I_m/I_0 = (1 + \mu_2/\mu_1)/(1 - e^{-(\mu_1-\mu_2)}) = (1 + e^{-\lambda})/(1 - e^{-(\lambda-\nu)}), \tag{14}$$

from which it is clear that this ratio always exceeds unity and increases with ω. However, if we use equation (4) instead of (5), we find, after making an expansion,

$$I_m/R_c = (1 + e^{-\lambda})\, e^{-\lambda/(e^{\lambda}-1)} - \frac{1 + e^{-\lambda}}{1 - e^{-\lambda}}\,[1 - (1 + e^{-\lambda})\, e^{-\lambda/(e^{\lambda}-1)}]\,\nu. \tag{15}$$

Now for positive λ, the term independent of ν increases monotonically from $2/e$ when $\lambda = 0$ to 1 when $\lambda = \infty$. Since this is the case, it follows further that the coefficient of ν is always negative for all values of λ whence, for a given ratio μ_1/μ_2, the less nearly normal the accommodation, the lower will be the amplitude of the stimulating alternating current, at optimal frequency, in units of the observed rheobase. Coppée (1936), for example, reports ratios of from 70% to 80%, and while Hill, Katz, and Solandt (1936) regard the experimental procedure as faulty, such values may, as we see, be regarded as an indication of non-normality of accommodation, especially in view of the fact that these investigators themselves find ratios which are below their expectations.

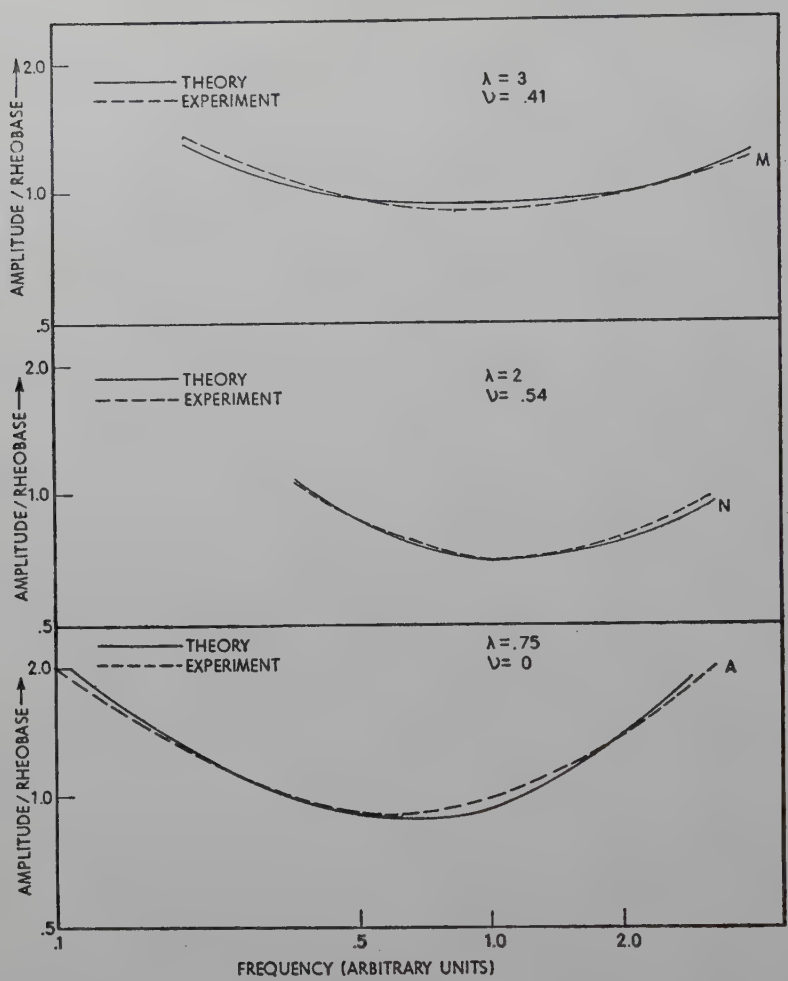

FIGURE 1

In Figure 1 three sets of Coppée's (1936) experimental data are compared with theoretical predictions, and the values of λ and ν are indicated. In the case of Coppée's fourth curve, no satisfactory fit was obtainable, even with corrections of higher order in ν, so that evidently other factors are involved. Nevertheless, it is clear that low experimental values of the optimal amplitude can be quite well accounted for by the two-factor theory, although, of course, deviations in other respects may occur as in the case of Coppée's fourth curve.

In making this comparison the experimental values were measured on the graph as published, since tables were not given, and the

plot was made doubly logarithmic for convenience of fitting. In this way it is possible to draw a set of theoretical curves with different values of λ, and by horizontal and vertical translations choose that one which fits most nearly. This determines λ. The height of the minimum then determines ν, and its abscissa could be used to determine the time-unit. These computations were made by Mr. Manuel Schwartz.

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CONTRIBUTIONS TO THE MATHEMATICAL BIOPHYSICS OF VISUAL AESTHETICS

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An expression for the intensity of central excitation corresponding to the perception of an angle is derived. A general expression for the aesthetic value of certain types of polygonal patterns is derived therefrom and compared with experimental values obtained by the rank order method. The theory is found to agree with the experiment within a limit of about 10%.

In a previous publication (Rashevsky, 1942, p. 179) we have discussed the relation of the intensity S of the peripheral stimulus corresponding to the perception of an angle ϕ, to the angles θ_1 and θ_2 which characterize the position of the sides of ϕ with respect to the vertical. Consider the simpler case that the stimulation is the same every time that the vertical (or horizontal) component increases or decreases by the same amount, and that the coefficient of proportionality a' is the same for the vertical and horizontal component. Then we find:

$$S(\phi) = a'(|\sin\theta_2 - \sin\theta_1| + |\cos\theta_2 - \cos\theta_1|). \tag{1}$$

In another publication (Rashevsky and Brown, 1944), we have shown that the central excitation increases as the square of the peripheral intensity S. Hence, with a as another coefficient, we find for the intensity of excitation of the center corresponding to the perception of an angle ϕ the expression:

$$e_{A\phi} = a(|\sin\theta_2 - \sin\theta_1| + |\cos\theta_2 - \cos\theta_1|)^2. \tag{2}$$

It has been suggested (Rashevsky, 1942, pp. 189-190) that relations such as equation (2) may be checked experimentally by measuring aesthetic values of polygons in which lengths and positions of straight lines in the plane do not vary, but angles do. This is obtained by permuting the sides of a polygon, leaving, however, the direction and length of each side invariant. Thus, starting with the 16-sided polygon shown in Figure 1a, we may obtain by permutation of the

a b c

FIGURE 1

sides such polygons as shown on Figures 1b and 1c, and a large number of other widely different shapes. For all such polygons the number and the intensities of excitation of all L-centers, V-centers, and H-centers (Rashevsky, 1942) are the same. However, the symmetry relations may change from case to case. Some of the polygons have a central symmetry, like Figure 1a. Some have a vertical and horizontal axis of symmetry, but no central symmetry. Some have only a vertical axis of symmetry. Some may have no symmetries whatsoever. A total of 77 polygons obtained by permuting the sides of Figure 1a were used in an experimental study of their aesthetic values by the rank order method. All 77 polygons had a vertical axis of symmetry, but not all had a horizontal.

Consider the general expression, derived previously [Rashevsky, 1942, equation (28)], for the total intensity E of central excitation, corresponding to a pattern of n elements. With the same notations as before, we have:

$$E = \sum_i n_i e_i - (n-1) \sum n_i e_i b_i , \tag{3}$$

with

$$n = \sum_i n_i . \tag{4}$$

The n elements constituting a pattern are divided into different groups such as the A-centers, L-centers, V-centers, etc. It is plausible to assume that while the inhibitory coefficients b_i will be different for different groups, they will be the same for the centers of the same group. We shall therefore denote by n_{ki} , b_{ki} , e_{ki} the quantity referring to the i-th neuron center of the k-th group. (Thus $k = 1$ may stand for the group of A-centers, $k = 2$, for the group of L-centers, etc.) Then, assuming that $b_{ki} = b_k$ is constant for a constant k , we have from equation (3):

$$E = \sum_k [1 - (n-1)\, b_k] \sum_i n_{ki} e_{ki}, \tag{5}$$

$$n = \sum_k \sum_i n_{ki}. \tag{6}$$

If we consider a set of polygons in which all symmetries are the same, and only the angles vary, then n is constant throughout the set. The sums $\sum_i n_{ki}\, e_{ki}$ are also constant; all except the one referring to the angles. Denoting now by b_A the value of b_k for the groups of A-centers, and correspondingly putting for that group $n_{ki}\, e_{ki} = n_A\, e_{Ai}$, we now find, with C as a constant:

$$E = C + [1 - (n-1)\, b_A] \sum_i n_A\, e_{Ai}. \tag{7}$$

But n_A is known, being the total number of angles, and e_{Ai} is given by equation (2), where ϕ is the value of the i-th angle. For every polygon the quantity $\sum_i n_A\, e_{Ai}$ can thus be calculated, and the observed aesthetic value should be a linear function of that quantity within a set of polygons with same symmetry relations. For sets with different symmetry relations, the values of n will be different, because of different numbers of symmetry centers. Therefore, for different sets the slope of the straight line should be different, and the value of C, which is also a function of n, should vary also from set to set. From the slopes and intercepts of the straight lines for sets with different values of n it is possible to determine the values of the different b_k's.

The experimental procedure was the same as that used in a previous study (Rashevsky and Brown, 1944), except that all the polygons were printed on square cards, 12 × 12 cm. The length of each side was 1.2 cm. A total of 109 subjects was used. The linear relation (7) was thus confirmed experimentally. Within the accuracy of the experiment it was found that the slopes and the intercepts of the straight lines were the same for all groups, except the ones with central symmetry. In the latter the slope is the same, but the value of C is greater. This means a very small value of b_A, and a large value of e_i for the center of perception of central symmetry. In order to obtain the values of b_A from such experiments, it will therefore be necessary to use polygons with many more sides so as to increase n.

Due to the above simplification, caused by the smallness of b_A, we may use the expression

$$E = C_1 + C_2 + C_3 \sum_i n_A\, e_{Ai}, \tag{8}$$

where $C_1 = 0$ except for polygons with central symmetry. The quan-

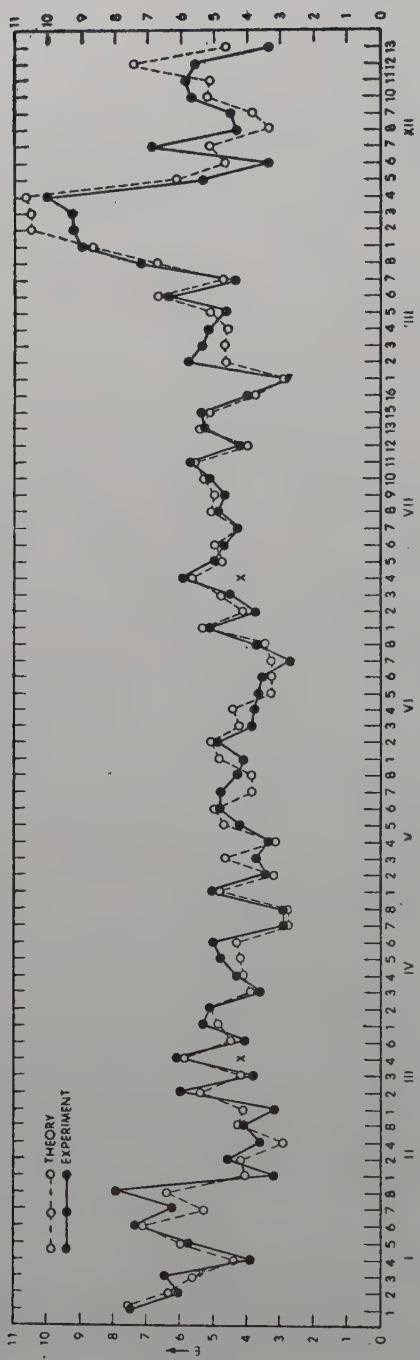

FIGURE 2

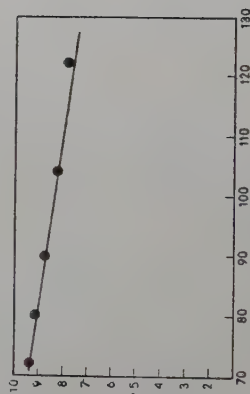

FIGURE 3

tity $\sum n_A e_{Ai}$ is calculated from equation (2), and contains still the factor a.

In Figure 2, the full line connects the experimentally observed aesthetic values; the broken line, those calculated from equation (8), with $C_1 = 1.9$; $C_2 = 2$; $aC_3 = 0.11$. The average difference between the observed and calculated value is 10.5%. The most frequently occurring difference is below 5%.

A remark must be made about polygons III-4 and VII-4. None of them has a central symmetry, but III-4 has a full horizontal symmetry, while VII-4 has even no horizontal symmetry. The theoretical values of E computed for those polygons with $C_1 = 0$ are, however, much too small, as shown by the crosses on Figure 2. If, however, we compute the value of E with $C_1 = 1.9$, as if they had central symmetry, the agreement becomes very good. The reason for this is that both polygons while not *exactly* centrally symmetric, are approximately so. The deviations from central symmetry fall apparently for many individuals within the limits of discriminal error.

The theoretical values for polygons XII-2, XII-3, and XII-4, as shown on Figure 2, have been corrected for end-effects of the rank order scale.

Now consider the polygon of Figure 1a, and derive from it a set of polygons in which the eight sides of the sharpest four angles have the same length l, while the remaining eight sides have all a different length l. All angles and symmetry relations are the same for all polygons of each set. By the same argument as before, we would expect now the aesthetic value E to be a linear function of $\sum_i n_L l_L$, where the subscript refers to the L-center. But $\sum_i n_L e_L$ is now proportional to $8l_0^2 + 8l_1^2$. Hence, denoting by A_1 and A_2 two constants:

$$E = A_1 + A_2(l_0^2 + l_1^2). \tag{9}$$

Figure 3 shows to what extent relation (9) is satisfied. The negative slope of the line indicates a large b_L, since A_2 is proportional to $1 - (n - 1)b_L$.

The authors are indebted to Miss Marianne Yampolsky for help in recording the experiments and in carrying out the computations.

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